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*Vascular* published online 22 April 2014  
DOI: 10.1177/1708538114532084

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# Advancements in identifying biomechanical determinants for abdominal aortic aneurysm rupture

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## Abstract

Abdominal aortic aneurysms are a common health problem and currently the need for surgical intervention is determined based on maximum diameter and growth rate criteria. Since these universal variables often fail to predict accurately every abdominal aortic aneurysms evolution, there is a considerable effort in the literature for other markers to be identified towards individualized rupture risk estimations and growth rate predictions. To this effort, biomechanical tools have been extensively used since abdominal aortic aneurysm rupture is in fact a material failure of the diseased arterial wall to compensate the stress acting on it. The peak wall stress, the role of the unique geometry of every individual abdominal aortic aneurysm as well as the mechanical properties and the local strength of the degenerated aneurysmal wall, all confer to rupture risk. In this review article, the assessment of these variables through mechanical testing, advanced imaging and computational modeling is reviewed and the clinical perspective is discussed.

## Keywords

Abdominal aortic aneurysm, biomechanics, peak wall stress, wall properties, wall strength, rupture risk

## Introduction

Abdominal aortic aneurysms (AAAs) represent a focal, balloon-like dilation of the aorta exceeding 1.5 times its normal diameter.<sup>1,2</sup> Therefore, in clinical practice, a 3-cm maximum diameter can be used to set the diagnosis of AAA. It is reported that 4–8% of men and 0.5–1% of women above 50 years of age bear an AAA.<sup>3,4</sup> Rupture represents the most catastrophic complication of the aneurysmal disease that is accompanied by a striking overall mortality of 80%.<sup>5–8</sup> Diagnostic and therapeutic protocols that regard AAAs aim in the prevention of such a disastrous scenario. Elective repair with open surgical intervention is being performed for decades with a continuously declining operative mortality.<sup>9,10</sup> Moreover, the advent of endovascular aneurysm repair seems to offer further advantages in terms of reduced adverse operative outcomes.<sup>11,12</sup> On the other hand, despite the technological progress and accumulated experience, current repair techniques are not without complications and taking into account that most AAA patients are elderly with several co-morbidities, the clinicians often have to answer the question when the risk of rupture and subsequent mortality justifies

the risk of surgical intervention.<sup>13–15</sup> Current guidelines for AAA management consider aneurysm size, as it is defined by its maximum diameter as well as aneurysm growth rate as the only variables to determine the need for elective repair. Therefore cut-off points have been set by the European Society for Vascular Surgery (ESVS), the American Heart Association (AHA) and the Society for Vascular Surgery (SVS) (maximum diameter  $\geq 5.5$  cm, growth rate  $\geq 1$  cm/year) that are generally thought appropriate for intervention to be recommended. Abovementioned societies consider that female patients generally need to be referred to a vascular surgeon at a lower threshold of maximum

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diameter while the ESVS guidelines specify this threshold at 5.2 cm.<sup>16,17</sup> Nevertheless, these certain cut-off points represent mean values that have emerged by large randomized trials and even though they can provide a general estimation of AAA risk of rupture they often have been proven unreliable and misleading for the treating physician. This is underscored by autopsy studies which indicate that small AAAs can rupture while some larger, well above the threshold for surgical repair remain intact for long time intervals that often exceed life expectancy of patients.<sup>18–20</sup> In fact, in the literature it is reported that up to 13% of AAAs with maximum diameter < 5 cm can rupture whereas the 50% of large AAAs never proceed to rupture.<sup>21,22</sup> Subsequently, the use of “one-size fits all” variables to evaluate AAAs often fails since it does not take into account each AAAs unique characteristics that may play a significant role in its evolution.

Laplace’s law that is believed to be the theoretical basis of the maximum diameter criterion states that stress acting on the aneurysmal wall is proportional to its diameter. This has been proven insufficient to describe AAAs behavior since the complex geometry of every individual AAA is far beyond a simple cylinder or sphere for which the abovementioned law is valid.<sup>23</sup> Furthermore, since aneurysmal disease mainly represents a degenerative process, the altered mechanical properties and reduced strength of the diseased arterial wall should be taken into account along with the stress exerted on it, to accurately estimate risk of rupture. Towards an individualized method to evaluate susceptibility to rupture, the biomechanical approach considers this unfortunate event as a material failure that occurs when the mechanical stress acting on the aneurysm wall overwhelms its strength.<sup>24</sup> Accordingly, wall stress and strength represent two essential variables for a biomechanically sound rupture risk estimation to be made.

In this review article, initially the role of wall stress is discussed and main landmark studies to assess its value are reported in a chronological order. Wall stress has been thoroughly studied in the literature and currently there are algorithms to estimate its distribution using in-vivo acquired data. On the other hand, this is not the case for wall strength and mechanical properties which are mainly addressed ex-vivo using mechanical testing. Therefore, their estimation although crucial to determine AAAs natural history and rupture risk profile, currently is not straightforward. In this regard, research that evaluates the importance of such properties along with the potential for their possible in-vivo assessment using imaging modalities is then discussed. The principal source of references employed MEDLINE searches with terms regarding clinical topics as well as basic research (abdominal aortic aneurysm, intraluminal

thrombus, computational modelling, biomechanical analysis, wall stress, wall strength, mechanical properties, elasticity, stiffness, distensibility, morphometrics, geometry, finite element analysis (FEA), fluid structure interaction (FSI), ECG-gated CT). We generally attempted to include references published after 2005 but there were earlier publications which either had a significant impact on current AAA management or consisted pioneer work which guided modern research, that were also included. Most recent article referenced was published at April 2013. Results were restricted to English language publications. Non-indexed citations, comments, letters and book chapters were not included in the current review article.

## Assessment of wall stress

### The role of peak wall stress

Stress is a measure of the internal forces induced per unit area of the arterial wall due to blood pressure and flow. Pressure-induced, in-plane wall stress is the dominant stress that produces the wall deformation while the flow induced shear stress is orders of magnitude smaller and therefore unlikely to influence AAA biomechanical behavior.<sup>25</sup> Consequently, the majority of computational studies quantify and compare the pressure-induced wall stress with the reported failure strength. In stress analysis, solid stress is numerically estimated based on the material’s constitutive law (stress–strain relationship) and the equations of mechanical equilibrium and conservation of momentum. Arterial wall stress distributions for uniform (FEA), as well as non-uniform (FSI), pressure wall loading are presented using the von Mises stress that is expressed as  $\sigma_{VM}$

$$\sigma_{VM} = \sqrt{1/2[(\sigma_1 - \sigma_2)^2 + (\sigma_1 - \sigma_3)^2 + (\sigma_2 - \sigma_3)^2]}$$

where  $\sigma_1, \sigma_2, \sigma_3$  are the principal stresses. PWS refers to the mechanical load sustained by the AAA wall, during maximal systolic pressurization. Its value depends on arterial systolic pressure, the mechanical properties and the geometric configuration of the material under study.<sup>24,26</sup>

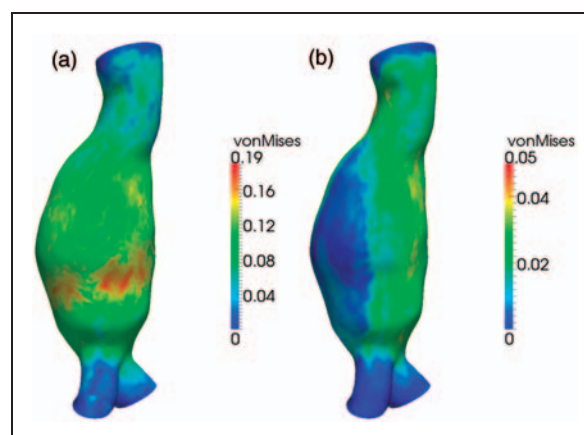
The first studies of wall stress estimation used idealized AAA models with spherical or cylindrical geometry. Simplified two-dimensional (2D) analysis indicated that maximum stress was proportional to aneurysm size and was exerted on the site where maximum diameter was located.<sup>27</sup> Others indicated that intraluminal thrombus (ILT) may reduce maximum stress values by up to 30%, whereas an important effect of AAA shape to magnitude and distribution of

wall stress was also recognized.<sup>23,28,29</sup> These studies fail to demonstrate actual distribution of wall stress throughout the AAA surface since the 2D simplified geometries can diverge a lot from patient-specific three dimensional (3D) AAA geometries.<sup>30</sup> Subsequently, Vorp et al.<sup>31</sup> performed stress analysis in hypothetical 3D AAA models to determine effect of aneurysm size and asymmetry on wall stress distribution. They suggested that maximum stress increased with increased diameter and high asymmetry, thus indicating that size is not the only determinant of the magnitude of wall stress since a similar effect of asymmetry was recognized. Therefore, similar-sized AAAs that according to the maximum diameter criterion would share the same rupture potential may in fact encounter different risk due to differences in the unique geometry of every AAA.<sup>31</sup>

Consequently, patient-specific AAA geometries with data derived from computed tomography (CT) were evaluated to determine wall stress distribution and PWS values. Fillinger et al. calculated AAA wall stresses in vivo for ruptured, symptomatic and electively repaired AAAs with 3D computer modeling techniques, CT scan data and blood pressure and indicated a higher PWS for ruptured and emergent symptomatic than for electively repaired aneurysms without any significant differences in maximum diameter or blood pressure. In their series, the smallest ruptured AAA was 4.8 cm, but this aneurysm had a stress equivalent to the average electively repaired 6.3 cm AAA. The same research group proposed that for AAAs under observation, PWS seems superior to diameter in differentiating patients who will experience rupture. PWS differentiated aneurysms with high rupture potential with 11% increased specificity and 13% increased sensitivity compared to the maximum diameter criterion.<sup>32,33</sup> Despite these novel and promising results, Fillinger et al. did not take into account the presence of ILT in their analysis, which as already reported has been suggested to significantly influence magnitude and distribution of wall stress.<sup>28</sup> Venkatasubramaniam et al.<sup>34</sup> also indicate an increased PWS for ruptured AAAs and furthermore they show that the location of AAA rupture correlates with the location of PWS. Moreover, it has recently been proposed that high wall stress at the shoulder of the aneurysm can identify those AAAs that are prone to rapid enlargement.<sup>35</sup> These studies are constrained by the model and material assumptions that are being taken into account for wall stress estimation, which can significantly influence obtained results. Wall thickness, mechanical properties and the assumption of zero stress at the diastolic phase all represent possible limitations of the abovementioned studies. Recently, in addition to rupture risk, high PWS has also been correlated with an increased growth rate

of small AAAs.<sup>36</sup> On the other hand, the same research group postulated that the amount of ILT inside the aneurysmal sac of an AAA may be a better predictor of rapid expansion than PWS values, thus indicating that despite the critical role of wall stress in aneurysms evolution, other parameters are also important.<sup>37</sup> Other investigators have reached similar conclusions indicating a potential of rapid expansion and rupture for AAAs containing large amounts of ILT compared to those with less or no ILT.<sup>38,39</sup> FEA on the other hand indicates a relevant role of thrombus demonstrating that incorporation of the ILT to the 3D stress analysis models of AAA has a profound influence on the magnitude and distribution of stresses with an overall reduction of the latter and a subsequent biomechanical cushioning effect of ILT as presented in Figure 1, which suggests a possible protective effect with regard to rupture risk.<sup>40,41</sup> Nevertheless, ILT has been shown to allow the transmission of luminal pressure to the aneurysm wall.<sup>42</sup> Furthermore, ILT fissures extracted from CTA data have been shown to locally increase the mechanical stress in the underlying wall by up to 30%. More importantly, ILT fissures that reach the wall or involve large parts of the ILT result in an increase in wall stress which could possibly cause AAA rupture.<sup>43</sup> Therefore while there is general agreement that there is a significant role of ILT in AAAs natural history, its exact effect is not clearly understood and remains to be further examined.

It should be noted that while most computational studies on AAA wall stresses utilize a uniform peak systolic luminal pressure, the pressure is actually not uniform along the aorta due to the blood flow.



**Figure 1.** (a) AAA wall stress distribution using finite element analysis for a patient-specific geometry without taking account the ILT. (b) As seen in the color scale, the magnitude of wall stress is markedly reduced when ILT is incorporated in the estimation of wall stress suggesting a biomechanical cushioning effect of thrombus.

In order to capture the fluid dynamics inside a complex AAA structure accurately and obtain a more realistic pressure distribution along the AAA luminal surface, dynamic simulations using the FSI approach have been developed. One of the pioneering works using this approach showed that the complex hemodynamics considerably affect the stress distribution.<sup>44</sup> In this regard, PWS values up to 20% higher compared to static FEA have been obtained.<sup>45</sup> Others that compared the stresses between FSI and FEA models reported that the combination of pulsatile flow and a compliant wall can change the local stresses slightly but has a negligible effect on the PWS.<sup>46</sup> In general, the addition of blood flow is physiologically more realistic and advantageous to structural analysis alone, but the potential benefit of accurately predicting AAA wall stress versus the increased computational time has yet to be proven useful in a clinical setting. Moreover, several assumptions that are being taken into account in FEA and FSI computational models are likely to influence obtained results which is a limitation of stress analysis in general.<sup>47</sup> Specifically, model assumptions such as whether arterial wall is considered a simple linear elastic or a realistic non-linear hyperelastic material, mechanical assumptions i.e. if a linear AAA geometry or a non-linear deformable geometry is adopted as well as taking into account pre-stressing, presence of ILT and calcification can lead to differences between calculated PWS values of 170% on average.<sup>47</sup>

### *The relation of geometric indices with PWS*

As already demonstrated, wall stress exerted on the AAA wall varies significantly among cases due to the special geometric characteristics of each individual AAA. Various research groups have explored the relation of specific geometric indices to PWS values and subsequent risk of rupture to define easily identifiable morphometric characteristics of AAA that may foretell a higher risk profile.<sup>48–51</sup> Giannoglou et al.<sup>48</sup> reported a strong relationship between PWS values and the centerline curvature in AAA models. Doyle et al.<sup>49</sup> on the other hand, identified centerline asymmetry as an important determinant of PWS values. Despite the importance of obtained results, these studies neglected the presence of ILT which as previously mentioned could greatly have influenced calculations of wall stress. Georgakarakos et al.<sup>50</sup> on the other hand recently reported a correlation between PWS and centerline tortuosity, based on computational models that take into account the presence of ILT. Furthermore, Xenos et al.<sup>51</sup> related wall stress with an increase of the iliac angle. Specifically, the increase in the iliac bifurcation angle was constantly associated with high stress values in this area, whereas an overall decrease of

the mean stress values in the rest of the AAA wall was revealed.<sup>51</sup> The authors postulated that there may be a remodeling adaptation mechanism that increases the iliac angle in order to reduce the mean stresses within the wall, as well as the PWS in the interim and that this is an attempt of the vasculature involved (the abdominal aorta and its branching iliac) to reduce the wall stresses, thus risk of rupture of the aneurysm itself, by transferring part of the load to the iliac. In turn, this may lead to an iliac aneurysm that is sometimes observed in patients with increased iliac angulation.<sup>51</sup>

### **Wall mechanical properties and wall strength**

#### *Ex vivo research to define natural history of AAAs*

It has long been recognized that aneurysmal disease is mainly a degenerative process affecting the arterial wall. Various pathology studies defined loss of structural integrity as a crucial determinant of AAA formation and evolution. Sumner et al.<sup>52</sup> were the first to demonstrate that aneurysmal segments of a vessel were stiffer and contained less collagen and elastin than the adjacent non-aneurysmal aortas. In agreement to these findings, He and Roach<sup>53</sup> indicated that both the composition and mechanical properties of AAAs are different from those of normal aortas and that aneurysms were stiffer. They found that while volume fractions of collagen and ground substance were increased, volume fractions of elastin and muscle were decreased in aneurysms.<sup>53</sup> Furthermore, Sakalihasan et al.<sup>54</sup> postulated that a significant correlation could be established between aortic diameter, increased collagen extractability and decreased elastin content. The reduced elastin concentration during the early development of the aneurysm without a concomitant reduction of collagen concentration represents a significant modification of the composition of the aortic wall and depends upon a specific degradation of elastin. The increased extractability of collagen, most obvious in the ruptured specimens, might reflect an accelerated turn-over rate and could result from a destabilization of the polymers after partial collagenase activity, leaving the cleavage products loosely associated to the fibers. Conclusively, most authors agree that biomechanical changes associated with aneurysmal diseases, include elastolysis which leads to aneurysmal-like dilation and collagen failure that is a necessary precursor to rupture.<sup>54,55</sup> Recently, mass fraction analyses suggested that there is pronounced higher elastin content as well as lower dry weight percentage of collagen within the AAA wall for females compared to males. Increased elastin may explain lower risk for AAA growth in females in the same time that decreased collagen may



have implications to their higher AAA rupture risk.<sup>56</sup> Specifically lower collagen generally leads to wall stiffening, which has been suggested to indicate a high-risk profile.<sup>56,57</sup> Finally, it has now been recognized that histopathology changes that relate to AAAs evolution may not be uniform throughout the entire aneurysmal wall. Specifically pathology studies suggest that the lateral aortic regions better reflect the inflammatory status of the wall thus being more rupture-prone.<sup>58</sup>

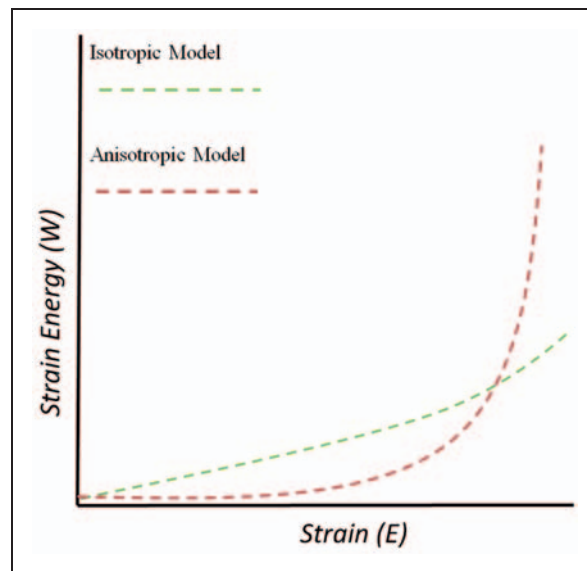
### Mechanical properties for FEA

Mechanical properties of AAA wall are essential for both stress analysis, since they represent a crucial parameter in FEA models, and for the estimation of the second determinant of the arterial wall failure that is its strength. Such properties have been determined from ex-vivo mechanical testing and their values represent mean values derived from large-scale population tissue mechanical studies. In most studies, the AAA wall has been assumed to be hyperelastic, incompressible and isotropic material as described by Raghavan and Vorp.<sup>32–36,41,50,59</sup> These authors suggested that previous utilized models which assumed linear elasticity are not appropriate for the AAA wall since ex vivo experiments show that the aneurysmal tissue is materially non-linear and undergoes large strains of the order of 20-40% prior to failure.<sup>59</sup> Therefore they developed a new finite strain material model for AAA based on experimental data.<sup>59,60</sup> Defining  $W$  as the strain energy density and  $I_B$  as the first invariant of the stretch tensor, the data from uniaxially loaded AAA specimens were reanalyzed to obtain a corresponding relationship between  $[dW/dI_B]$  and  $[I_B-3]$ . It was determined that  $[dW/dI_B]$  varies linearly with  $[I_B-3]$  ( $R^2 = 0.99$ ). Therefore if  $\alpha$ ,  $\beta$  are the model parameters indicative of the mechanical properties of AAA wall, the proposed strain energy function would be

$$W = \alpha(I_B - 3) + \beta(I_B - 3)^2$$

The model has only two parameters and is easy to employ in the stress analysis of AAA.<sup>59</sup>

More recent research applied bi-axial instead of uni-axial testing in aneurysmal wall specimens and indicated that tissue exhibited anisotropic exponential response. The difference between the isotropic and anisotropic relation was tested and the marked difference in mechanical response of the tissue between the two models demonstrated the importance of correct model choice in biomechanical simulations.<sup>61</sup> A graphical representation of how the averaged isotropic relation and the averaged anisotropic constitutive relation

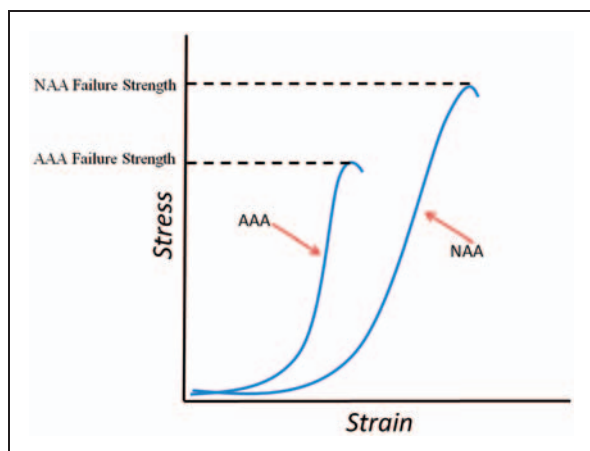


**Figure 2.** A graphical representation of how the averaged isotropic relation and the averaged anisotropic constitutive relation for AAA strain energy versus equibiaxial strain fit into AAA models. The isotropic model displays significantly larger strain energy at lower strains.

for AAA strain energy versus equibiaxial strain fit into AAA models is presented in Figure 2.

### Ex vivo mechanical testing to estimate arterial wall elastic properties and strength

Various pathology studies examined mechanical properties of aneurysmal aortic wall and compared to that of normal aorta to define differences that accompany AAA formation and evolution. Elastic properties as well as strength of aneurysmal tissue have been thoroughly investigated through ex vivo mechanical testing. Vorp et al. found an almost 50% reduced strength of AAA wall compared to normal aorta, which in the same time was found to be significantly stiffer.<sup>62</sup> Accordingly a more recent study by Xiong et al. indicated that elastic moduli of AAA were greater than those of the non-aneurysmal walls.<sup>63</sup> Examining the stress-strain curves between AAA and normal vessel walls they found considerable differences.<sup>63</sup> Although the shape of the curves was similar for both kinds of tissue, in AAAs the former was shifted to the left and possessed a greater slope which suggested that the AAA wall is stiffer and less distensible under the ultimate stress.<sup>62</sup> A graphical representation of this conception is presented in Figure 3. Furthermore, Di Martino et al compared aneurysmal tissue from electively repaired and ruptured AAAs to determine changes in wall properties that may accompany rupture.<sup>57</sup> Their data indicated that rupture is associated with aortic wall weakening, but not with wall stiffening.<sup>57</sup> Reduced



**Figure 3.** A representation of stress–strain curves for abdominal aortic aneurysm (AAA) and non-aneurysmal aorta (NAA). Aneurysms are stiffer than the unaffected vessel presenting a lower point of failure strength.

strength of aortic wall in ruptured AAAs was related to increased wall thickness and decreased stiffness but not to AAA maximum diameter and therefore the authors postulated that these parameters may be better predictors of rupture for large AAAs.<sup>57</sup>

With concern to wall strength a spatial distribution along the surface of the AAA has been recognized. In an autopsy study, there was neither a marked difference in wall thickness between small and large AAAs, nor in failure tension, perhaps due to a remodeling phenomenon in large AAAs. It seems that rupture is a localized process, making the identification of possible rupture sites difficult, and surely not always identical to the location of PWS.<sup>64</sup>

Furthermore, ILT has been reported to have a negative effect on wall strength inducing localized hypoxia.<sup>62</sup> Regions of thicker ILT present mural neovascularization, inflammation, as well as regional wall weakening that is observed in an ILT-thickness-dependent manner.<sup>65</sup> Others highlight the role of enzymatic activity and postulate that matrix metalloproteinase-2 (MMP-2) is implicated in the degradation of elastin in the small AAAs wall, leading to enlargement, whereas the increased expression of MMP-9 leads the rupture of the larger AAAs.<sup>66</sup> Vallabhaneni et al. suggested that the spatial variation in wall strength was linked to variations in matrix metalloproteinase production.<sup>67</sup>

In an effort to non-invasively estimate wall strength that is an important determinant of rupture risk mathematical models for its prediction have been developed. Based on easily measurable parameters including local AAA diameter, local ILT thickness, patient age, patient gender and patient's family history of AAA disease, the

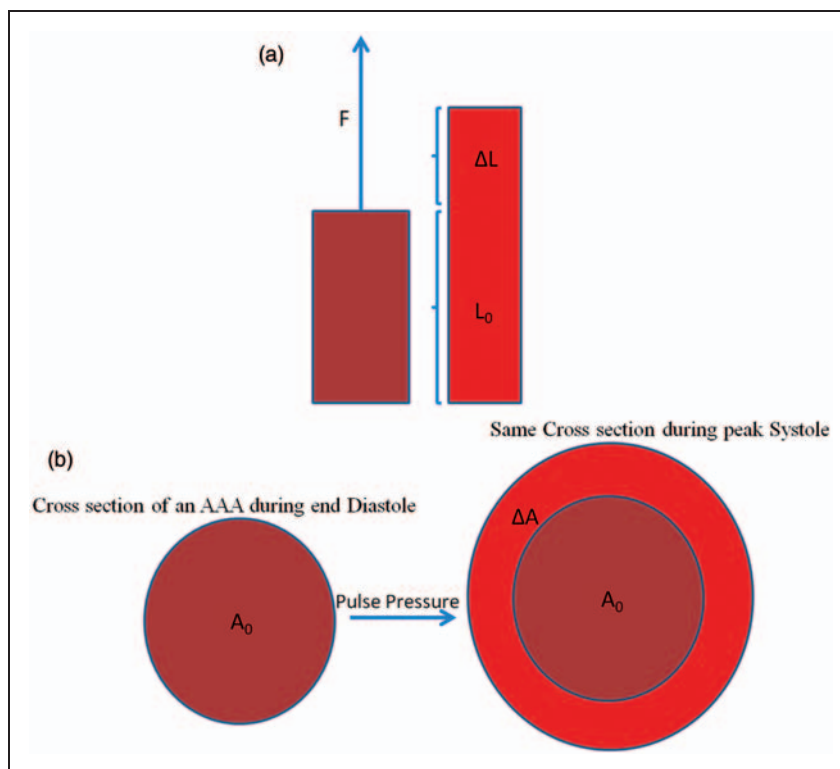
wall strength distribution along the AAA surface is estimated according to the mathematical type:

$$\begin{aligned} \text{STRENGTH} = & 71.9 - 37.9 \times (\text{ILT}/2 - 0.81) \\ & - 15.6 \times (\text{NORD} - 2.46) - 21.3 \times \text{HIST} \\ & + 19.3 \times \text{SEX} \end{aligned}$$

STRENGTH is the predicted strength of a point on the AAA wall in N/cm<sup>2</sup>, ILT is local attached ILT thickness in cm, NORD is the local diameter normalized to the diameter of non-aneurysmal aorta estimated from the patient's age and sex, HIST is family history (1/2=with, -1/2=without), SEX is patient's gender (1/2=male, -1/2=female).<sup>68</sup> This represents a statistical model to non-invasively estimate the distribution of AAA wall strength, comparing predicted values with actual values calculated from the tensile testing of surgically procured AAA wall specimens and using backwards-stepwise regression techniques to identify and eliminate insignificant predictors for wall strength.<sup>68</sup> Although useful, this model uses mean values and can diverge from actual values representing an indirect method to estimate wall strength in vivo. Specifically except from patient specific variables such as intraluminal thrombus thickness and normalized diameter, universal ones such as gender and family history are also being taken into account. These are unlikely to assist in patient-specific wall strength estimation leading to only a moderate correlation between predicted and ex vivo measured wall strength. Moreover, examined samples were only collected from the anterior region of AAA while ideally should be obtained from the anterior, posterior and lateral regions. Another important constraint of the model is that the range of the original data from which it was constructed limits its application and even negative values of wall strength can be obtained in a 'worst case scenario'. Finally the assumption that isolating and failing uniaxial strips of AAA tissue can adequately represent the true failure mechanisms of AAA is not necessarily valid.<sup>68</sup>

### *The advent of non-invasive estimation of wall properties in vivo*

Imaging techniques have been exploited in order to non-invasively obtain mechanical properties of AAA wall. This is based on recording the AAA deformation in vivo, under physiological conditions of systemic pressurization to inverse-estimate the material parameters resembling the ex vivo mechanical testing of aortic tissue as presented in Figure 4. Initially ultrasonography and more recently MRI as well as CT scan all have been used for this task. Most authors postulate an increased stiffness of the diseased aneurysmal portion



**Figure 4.** (a) Mechanical testing of excised aneurysmal tissue evaluates the deformation (elongation  $\Delta L$ ) due to the applied force ( $F$ ) to determine its elastic properties. (b) Imaging techniques that capture the in vivo deformation of the AAA wall during the cardiac cycle (change in vessel cross-sectional area  $\Delta A$ ) due to the systemic pressurization use this information to determine vessel elastic properties.

compared to the normal aortic segment in accordance to ex vivo mechanical testing.<sup>69–78</sup> Lanne et al. used ultrasound and indicated that the pressure strain elastic modulus and stiffness increased (i.e. compliance decreased) in an exponential manner according to age.<sup>69</sup> Furthermore they examined a group of 37 males with aneurysmal widening of the distal abdominal aorta and suggested a significant increase in stiffness when compared to an age-matched control group.<sup>69</sup> Vorp et al.<sup>62</sup> in an ultrasonography study indicated that aortic wall alone was less compliant than the luminal surface enclosed by ILT. They managed to non-invasively estimate thrombus compressibility and found thrombus area to remain nearly constant during cardiac cycle, thus postulating that intraluminal thrombus is incompressible.<sup>70</sup> Long et al.<sup>71</sup> suggested that compliance parameters can easily be measured during routine AAA ultrasound monitoring using the tissue Doppler imaging system. Their study showed an increase in compliance with increased AAA diameter. Moreover, they suggested that a change in dispersion of AAA distensibility may appear around 45 mm of diameter.<sup>71</sup> Sonesson et al.<sup>72</sup> even though indicating increased stiffness of the aneurysmal tissue compared to normal vessel, found no difference in mechanical

properties between ruptured and non-ruptured AAAs, thus proposing that it is not possible to use aneurysmal aortic wall stiffness as a predictor of rupture. On the contrary, Wilson et al.<sup>73,74</sup> in a prospective study that included 210 patients with AAAs suggested that changes in distensibility could assist in rupture risk estimations. Their patients when examined as cohort tended to present an overall decrease in distensibility over time. On the other hand, an increased distensibility at baseline and an increase in distensibility over time were observed in AAAs that went on to rupture. Finally, a recent study based on ultrasonography which examined 167 patients with AAA postulated that initial maximum diameter as well as baseline stiffness could predict the need for future surgical repair.<sup>75</sup> Their findings challenge the results of previous studies that indicate increased distensibility as a risk marker for high rupture risk and make clear that more data are needed for a better understanding of the effect of aortic wall elastic properties in the AAAs evolution and for the incorporation of such variables in the prediction models.<sup>75</sup> Ultrasound although extensively used to non-invasively assess AAA elastic properties has certain limitations. First, reliable information cannot be obtained from a significant minority of patients because



**Table 1.** Studies that attempted to estimate arterial wall mechanical properties non-invasively using imaging techniques. The year of the study, number of patients under examination, imaging modality used and main findings are reported.

Author and year of publication	Number of patients examined	Imaging modality used	Study conclusions
Lanne et al. 1992 <sup>69</sup>	37	Ultrasound	Significant increase in stiffness of abdominal aortic aneurysms (AAA) compared to normal aorta
Vorp et al. 1996 <sup>70</sup>	8	Ultrasound	Intraluminal thrombus (ILT) more compliant than AAA wall. ILT is incompressible.
Wilson et al. 1998 <sup>74</sup>	112	Ultrasound	Increased baseline compliance may indicate high risk profile
Sonesson et al. 1999 <sup>72</sup>	285	Ultrasound	No difference in mechanical properties between AAAs that eventually ruptured and those that remained intact
Wilson et al. 2003 <sup>73</sup>	210	Ultrasound	Increase in compliance with time may correlate with increased rupture risk
Long et al. 2005 <sup>71</sup>	56	Ultrasound	Distensibility of AAAs is positively correlated with maximum diameter
Ganten et al. 2007 <sup>76</sup>	31	ECG-gated CT	Age-dependent decrease of aortic wall elasticity
Ganten et al. 2008 <sup>77</sup>	67	ECG-gated CT	Reduced distensibility within AAAs compared to normal aorta. Lack of difference with AAA size suggests that this reduction occurs early in AAAs development
Hoegh et al. 2009 <sup>75</sup>	167	Ultrasound	Increased stiffness may foretell the need for surgical repair of AAAs
Trujers et al. 2009 <sup>82</sup>	17	ECG-gated CT	In-vivo ILT compressibility varies considerably from patient to patient. ILT might act as a biomechanical buffer in some, while it has virtually no effect in others
Marcel van de veer et al. 2010 <sup>83</sup>	10	ECG-gated MRI	A strong linear relationship between the intra-aneurysmal pressure and the volume change of the AAA.
Molacek et al. 2011 <sup>78</sup>	12	ECG-gated CT	Lumen distensibility is significantly higher than distensibility of the wall and ILT acts in this respect as a buffer.

of obesity, bowel gas, arrhythmia and inability to lie flat or hold the breath.<sup>79</sup> Additionally, the technique is associated with an important interobserver and intraobserver variation and is highly dependent on the operator.<sup>79</sup> Moreover, ultrasound measurements are unable to capture motion in three dimensions (usually only the longitudinal axis is used) and thus mechanical properties in every AAA segment. In this regard, AAA deformation cannot be recorded simultaneously in different parts of the wall and is usually captured at the point of maximal AAA diameter in longitudinal section. However, clinical experience and autopsy studies suggest that AAAs do not always rupture at this point.<sup>79</sup> These constraints are eliminated with the use of advanced imaging modalities currently available.

Ganten et al.<sup>76</sup> exploited modern imaging techniques to estimate mechanical properties of the normal aorta and the AAA. Using ECG-gated CT scan initially

they studied the age-dependent differences in distensibility of the suprarenal and infrarenal aortic portions. They recorded cross-sectional area changes of the vessel during cardiac cycle and using blood pressure data they calculated distensibility as the relative cross-sectional area change of the vessel during cardiac cycle divided by the blood pressure

$$D = \frac{[A_{\text{SYSTOLE}} - A_{\text{DIASTOLE}}]}{A_{\text{DIASTOLE}} \cdot \Delta P} = \frac{\Delta A}{A_0 \cdot \Delta P}$$

( $D$ : Distensibility,  $A_{\text{SYSTOLE}}$ : Vessel cross sectional area at peak systole,  $A_{\text{DIASTOLE}}$ : Vessel cross-sectional area at end diastole,  $\Delta P$ : pulse pressure).

They found differences between the ages, which were significant between the youngest and oldest third studied.<sup>76</sup> Moreover, using the same methodology they compared distensibility of normal aortic wall to that

of AAA indicating that the normal vessel is more distensible and can better withstand systemic pressure peaks, whereas the wall of the AAA is stiffer.<sup>77</sup> However, reduction of distensibility within aneurysms compared to normal proximal aorta is subtle; the lack of difference between both small and large aortic aneurysms suggests that this reduction occurs early in the aortic aneurysm's development.<sup>77</sup> In a more recent study, Molacek et al.<sup>78</sup> also exploiting ECG-gated CT scan found AAA lumen included by ILT to be significantly more distensible than AAA wall and proposed that thrombus acts in this respect as a buffer, thus inhibiting the effect of pulse waves on the wall.<sup>78</sup> Therefore, they hypothesized that from a mechanical point of view, the thrombus may act protectively against the risk of rupture. Despite the proved significant differences between distensibility of the AAA wall and normal aorta, values of AAA wall distensibility reached or even exceeded values of distensibility of the normal aorta above the AAA in some particular cases and this phenomenon was observed mainly in AAAs with rapid enlargement.<sup>78</sup> Although these studies use modern imaging modalities to non-invasively assess AAA wall elastic properties and in this regard they are advantageous to previous ultrasound based studies, they only take into account limited CT slices thus avoiding taking into consideration the entire aneurysm and record regional instead of universal properties. Moreover, despite comparisons between the unaffected suprarenal and the aneurysmal infrarenal aortic segment is an interesting concept, such comparisons may not display the extent of degeneration due to aneurysmal disease since non-aneurysmal supra- and infrarenal aortic portions present histopathologic differences. Specifically, there is an initial lower elastin content without a corresponding decrease in collagen and a lack of medial vasa vasorum of the infra-renal aorta which may make it structurally vulnerable to degenerative alteration and subsequent development of aneurysmal disease.<sup>80,81</sup> On the other hand, the possibility of an intra-patient variable comparing aortic elasticity above and below the renal arteries to assess the evolution of the degeneration due to AAA has to be validated by larger studies.

Other research groups evaluated ILT compressibility non-invasively and challenged findings of previous mechanical and ultrasound-based studies. A variation of thrombus compressibility from patient to patient was found, and this was irrespective of aneurysm size, pulse pressure and thrombus volume. Thus, it is proposed that ILT might act as a biomechanical buffer in some, while it has virtually no effect in others.<sup>82</sup>

MRI has also been used to capture aortic wall motion during cardiac cycle and estimate mechanical properties of AAA. Van't Veer et al.<sup>83</sup> managed to

calculate aneurysmal wall elastic properties and specifically compliance and Young's modulus by recording vessel volume change for 15 phases during cardiac cycle. Furthermore, they found a strong linear relationship between the intra-aneurysmal pressure and the volume change of the AAA.<sup>83</sup> The studies that attempted to estimate arterial wall mechanical properties non-invasively using imaging techniques as well as their findings are summarized in Table 1.

## Conclusion

### ***Towards an individualized model for AAA rupture risk estimation—a glimpse of the future***

Currently, the diameter criterion, being based on Laplace's law that predicts maximal stress in the segment of maximum size, is used to evaluate AAA risk of rupture and determine the need for surgical repair.<sup>16</sup> This has often been proven insufficient leading to both conservative treatment of AAAs below the threshold for intervention but still bearing a high risk potential and an unnecessary operative risk for larger AAAs that would otherwise never proceed to rupture.<sup>18–20</sup> Actually, aneurysmal disease represents a far more complex biological and biomechanical system and multiple factors may influence its evolution. In this regard, AAA geometry has been suggested to be important with more tortuous and asymmetric vessels having been hypothesized to have an increased rupture risk.<sup>48,50</sup> The role of ILT is certainly crucial but its exact effect has not yet been definitively determined. On one hand computational analysis indicates a buffering effect postulating a protective role of ILT.<sup>41</sup> On the contrary not only mechanical studies show that ILT leads to wall weakening but also models that calculate wall strength incorporate a content-dependent negative effect of ILT.<sup>65,68</sup> Moreover, observational studies show a higher ILT amount to coincide with faster growth and higher rupture rates which overwhelms its effect in reducing PWS.<sup>37–39</sup> These data tend to favor an overall negative effect of ILT which nevertheless has to be verified.

The biomechanical approach is based on physical principles and has been suggested to be far superior in evaluating rupture risk of AAAs than the universal maximum diameter criterion. Wall stress although sensitive to various model assumptions is a valuable variable in assessing susceptibility to rupture and can currently be estimated using data acquired in vivo.<sup>24</sup> Nevertheless, PWS alone is insufficient to predict rupture since the wall strength is not the same throughout the aneurysm wall. That is, the point of PWS could coincide with greater wall strength and mislead with concern to

actual rupture risk as well as sites inside the aneurysmal sac more prone to rupture. For an accurate prediction of AAAs rupture risk, a non-invasive mode to assess wall strength distribution similarly to that of wall stress is required. Only then the exact punctiform relative comparison of the two biomechanical determinants of rupture could be performed, for an accurate patient-specific prediction to be made. Ultrasound and recently modern imaging techniques, like MRI and ECG-gated CT, currently are exploited to capture aortic wall motion during the cardiac cycle, thus recording non-invasively, in vivo deformation of the AAA under physiological conditions to inverse-estimate the material parameters. Such research suggested a possible predictive role of aneurysmal wall elastic properties with respect to risk of rupture. Specifically, increased baseline distensibility as well as an increase in distensibility over time seem to indicate a high-risk potential.<sup>73,74,78</sup> Since the prompt relation of these parameters to actual wall strength has been postulated by various pathology studies, the estimation of the former through imaging techniques hopefully will result in the in vivo determination of aneurysm wall strength distribution throughout the AAA surface, non-invasively. This could lead to the direct, individualized, aneurysm rupture risk estimation based in the pointwise comparison of wall stress and strength beyond the “one-size fits all” maximum diameter criterion.

### Conflict of interest

None declared.

### Funding

The research project was partially supported by the Action «Supporting Postdoctoral Researchers» of the Operational Program “Education and Lifelong Learning” (Action’s Beneficiary: General Secretariat for Research and Technology), and is co-financed by the European Social Fund (ESF) and the Greek State.

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